REMARKS

I. Introduction

The prosecution of this case is beginning to have a long life - far too long! It was prosecuted through to a final rejection, a Notice of Appeal filed, and then an Appeal Brief filed; thereafter the Examiner withdrew the case from final rejection, issuing yet another rejection. Thereafter, the case was again prosecuted through to a final rejection of December 28, 2005. And, on March 28, 2006, the Examiner withdrew this final rejection issuing yet another non-final rejection of March 28, 2006, citing two new Chinese references! For the convenience of the office, the Chinese references have been translated and copies are enclosed. All other rejections of the claims except for the Chinese one are old rejections, having been repeated and answered several times. It is not believed that the Chinese references are any more relevant than the other references and this is especially made clear by the English language translations.

Likewise, the 35 U.S.C. § 112 rejection on the basis of indefiniteness for use of the language "small but nutritionally effective amount" has been previously treated several times. The law supports use of this time honored language and it has not been changed in this instance, either. The Examiner did make a new rejection to the word "containing" as indefinite. This has been obviated by adopting the Examiner's suggestion of changing "containing" to "having".

II. Claim Rejections - 35 U.S.C. 112, Second Paragraph

A. Small but Nutritional Supplementing Effective Amount

The Examiner's rejection of March 28, 2006 simply repeats the 35 U.S.C. § 112, second paragraph, objection of the first Office Action dated July 22, 2004. There the Examiner argued that the phrase "a small but nutritional supplementation effective amount" is vague and indefinite

because the terms "small" and "effective amount" do not state how much the effective amount can be (7/22/2004 Office Action, P2).

1. The Functional Phrase Here Selected is Time Honored and Case Law Approved

It has long been held, even by the predecessor of the Federal Circuit, the Court of Customs and Patent Appeals that phraseology such as "small" or "an effective amount" are not indefinite where the amount as such is not critical, even if the functional words are at the point of novelty (see *In re Halleck*, 164 U.S.P.Q. 647) (CCPA 1970). Similarly, in *In re Frederickson and Nelson*, 102 U.S.P.Q. 35 (CCPA 1954), the court said that a small but effective amount is an adequate description under paragraph 2 of 35 U.S.C. § 112 where the function of the active is stated. Here the function of the active is stated, i.e., a nutritional supplementation effective amount. To the same effect is a more recent case of *In re Watson*, 186 U.S.P.Q. 111 (CCPA 1975) pointing out that there is nothing indefinite about saying an effective amount if the stated function to be achieved is recited in the claim. Here the stated function is recited in the claim, i.e., a nutritional supplementation effective amount. Other cases could be recited but the point is made. The Examiner's rejection is erroneous. It should be withdrawn since the claim itself used a time honored and approved format, and since the stated function is in fact recited in the claim. There is nothing indefinite.

Finally, it is pointed out that the claims are to be interpreted in light of the specification and the specification itself provides not only the functional guidelines recited in the claims but also specific ranges (see Example 9, Table 2 for recommended feeding amounts at Specification, page 17).

B. The "Containing" Objection is Moot

The Examiner objected to the phrase in the claim "containing" as vague and indefinite and suggested changing it to "having". Applicant has adopted the Examiner's suggestion and this objection is therefore rendered moot.

III. Claim Rejections - 35 U.S.C. § 102(a)

1. Kirschner et al. (U.S. 6,352,713)

The Examiner has again rejected claims 1 and 2 under 35 U.S.C. § 102(a) over Kirschner et al. The rejection is traversed. It is the theory of the rejection that Kirschner discloses prenatal nutritional supplementation with a supplement containing "ferrous gluconate" for pregnant women. Further, according to the Examiner, the composition has as one intended usage in animal feed (see column 8, lines 65-66). The rejection is traversed.

A rejection under 35 U.S.C. § 102(a) for anticipation, such as made by the Examiner in the instant case, necessarily implies that the invention sought to be patented has been, "patented or described in a printed publication in this or a foreign country before the invention", and therefore is not "new", i.e., that there are no differences between what is claimed and what is disclosed in the prior art. Bearing this legal standard in mind, it is apparent that Kirschner et al. do not specifically name, describe or claim any particular, individual compound anticipating Applicants' claims; nor is there any suggestion by Kirschner that its iron compound is a neutral, 1:1 complex, and therefore capable of being used for any of Applicant's intended purposes, for example, meeting the dietary needs of humans and animals by providing a more bioavailable source of trace mineral.

The facts at hand are analogous to those presented in Application of Kalm, 378 F.2d 959 (CCPA 1967), a case of binding authority in this matter (a copy of which is enclosed for the Examiner's convenience). In Kalm, the claimed invention related to particular morpholine derivatives. Kalm, 378 F.2d at 960. Claim 3 was directed to the specific compound 2-cyclohexyl-3, 4-dimethylmorpholine. Id. According to the specification, Kalm's compounds were described as being useful as "selective central nervous system [CNS] depressants - being potent barbiturate potentiators." (Emphasis supplied). Id. According to Siemer, the compounds he disclosed had "a most marked anti-depressive action." Id. at 961.

The examiner rejected claims 1-3 under 35 U.S.C. § 102(e) as being anticipated by the Siemer patent. Kalm, 378 F.2d at 960-61. The CCPA (predecessor to the Federal Circuit) reversed the examiner and Board's rejection of the claims 1-3 under Section 102, stating that there appeared to be "no question that the Siemer patent does not specifically name, describe or claim any particular, individual compound anticipating appellant's claims, nor is there any suggestion by Siemer that any of his disclosed compounds is capable of depressing the central nervous system. Kalm, 378 F.2d 959, 962 (CCPA 1967). The Court noted that it was the Patent Office's position that Kalm's claimed compounds fell within the scope of the "genus" disclosed by Siemer. Id. at 962-63. The Court disagreed. Instead, the Court determined that Siemer's genus was limited to compounds possessing properties "diametrically opposite" to the properties possessed by Kalm's genus of compounds. Id. at 963. The Court added:

> While it is not necessary that a reference disclose every property or attribute of a composition of matter to be a valid anticipation, appellant has found properties for his claimed compounds which are totally incompatible and inconsistent with, not merely complementary or in addition to, those attributed by Siemer to his compounds. It is our view that Siemer never intended to, nor does he, disclose compounds within the scope of appellant's claims.

Id.

In the present application, the Examiner argues that one of the numerous iron compounds disclosed in Kirschner has "the possibility" of disclosing each and every limitation of Applicant's claimed compounds. (12/23/05 Office Action, p. 6). However, as noted above, it is not sufficient for the Examiner to demonstrate an outside possibility that something may anticipate in order to satisfy the legal burden under Section 102(a). In fact, there is no indication in Kirschner whatsoever that its iron compound is a neutral, 1:1 complex, as required by Applicants' claims. Kirschner therefore does not anticipate, and Applicants' respectfully request that this ground of rejection be withdrawn.

2. Henry, Jr. (U.S. 6,358,544)

It is the theory of Henry that it anticipates because it discloses "a zinc aspartate compound" (see col. 7, lines 13-16) to be used in the beverage dry mix (see col. 7, lines 16-27). The Examiner argues this is identical with the claim. It is not and therefore the rejection is traversed.

Claim 1 was rejected as anticipated by Henry. Applicants respectfully traverse this objection. It is the theory of the Examiner's anticipation rejection that Henry discloses a zinc aspartate compound (see column 7, lines 13-16) to be used in the beverage dry mix (see column 7, lines 16-27). The Examiner argues therefore Henry is identical with Applicants' claim 1. Henry states in column 7, lines 13-25, "the zinc compound which can be used in the present invention can be any of the commonly used forms such as" and then lists a variety of "commonly used" zinc forms including zinc aspartate. Most of the zinc forms listed are salts of zinc and not complexes. Henry, like Kirschner in the prior rejection, does not provide any information on the exact nature of "zinc aspartate." In examples 1-3 and 5-9, zinc gluconate is listed as the zinc form used. This is a salt of zinc and gluconic acid which contains one zinc ion for every 2

molecules of the gluconate anions. Henry's compound is not neutral as is Applicants'. The neutrality of Applicants' complex – one ion of an essential trace element for each molecule of the dicarboxylic α-amino acid – is the novelty which makes it highly useful. The term "neutral complex" represents a specific group of compounds in which the metal is bound to a ligand to form a stable entity that does not dissociate readily into its components. In contrast to complexes, salts are readily dissociated into its component ions. Individuals of ordinary skill in the art of chemistry readily recognize the difference between salts and complexes, and are able to decide which of these to use for a specific application. In no instance is a "neutral complex" taught to include salts. Therefore, a person of ordinary skill would readily differentiate between Henry, where a salt is used, and the present application where a neutral complex is used. Claim 1 is therefore not rendered obvious by Henry, and Applicants respectfully request this ground for rejection be withdrawn.

3. The Chinese References

Claims 1 and 2 were rejected as anticipated under § 102 over Li et al. on the basis that Li discloses zinc glutamate compound to be used for therapeutic purposes, and over Zhang under § 102(b). The Examiner urges that Zhang discloses the preparation of zinc aspartate and zinc glutamate as "zinc-supplying drugs". Full translations of the two Chinese references are enclosed for the convenience of the Examiner. An examination of the full translations makes it clear the identical compounds are not disclosed.

These articles describe compounds that are different than those described in the Applicants' patent application. The compounds described in these articles are water soluble as evident from the description of their method of preparation and as stated on page 2 of the 1997 article. The compounds described in Applicants' application are sparingly soluble in water

indicating different structure. To obtain their compounds the Chinese authors filtered the reaction mixture to remove the insoluble unreacted materials, concentrated the filtrate, added methanol and cooled the mixture to obtain the solid product. Her, the inventors simply mix the appropriate reactant under the specified conditions to obtain the products which are sparingly soluble in water and form a voluminous precipitate, another indication of different compounds.

The compounds described in these articles are "inner salts" of the amino acids as concluded by the authors from the examination of the infrared spectra of the compounds. The authors state on page 4 of the 1997 article *"These facts indicate that the amino acid in the compound is still present in the form of an inner salt. The oxygen atom in the carboxyl group forms bond with* Zn^{2+}*. The N atom does not participate in bonding. The displacement of the extended vibration of* NH_3^+ *is caused by a hydrogen bond of* H_2O*."* The compounds described in the present claims 1 and 2 are complexes between the amino acid and the metal ion. As stated in paragraph [0020] of the application *"Compounds described in this invention are neutral complexes of one of the essential trace elements such as copper, manganese and zinc with di-carboxylic α-amino acids such as glutamic acid and aspartic acid. The amino acid ligand is selected to serve a dual role, as the bidentate ligand that forms a complex with the metal ion, and as the counter ion to balance the charge on the cationic complex of the metal and amino-carboxyl moiety."* The structural assignment is based on the careful examination of the infrared spectra and other physical and chemical properties of the compounds described in our application. This quote if taken literally says the structures are different and not anticipating.

It is not surprising that the compounds described in the Chinese articles are different than the compounds described in our application since the authors of the Chinese articles used reactants and reaction conditions different than those used in the present application.

The Chinese articles do not describe the preparation of the compounds in sufficient experimental details to allow the reproduction of their experiments. They are therefore not enabling. This makes it impossible to physically compare the compounds obtained by reproducing their methods to the compounds described in our application. But the written description evidence shows they are different.

In summary, the Chinese articles offered nothing more than redundancy to the art already of record. They do not anticipate either the compounds, or their use as here claimed.

IV. The Obviousness Rejections Under 35 U.S.C. § 103(a)

1. Moore (U.S. 6,323,354)

The Examiner argues that Moore teaches transition metal chelates as palatable bioavailable sources and that it would be obvious to use dicarboxylic alpha amino acids as recited. The rejection is traversed.

Claim 1 is rejected as unpatentable over Moore. Applicants respectfully traverse this rejection. It is the theory of the Examiner that although the instant invention differs from this prior art in that the 1:1 neutral complex of an essential trace element and a dicarboxylic α-amino acid is recited, the instant application is unpatentable because it is possible that a skilled artisan in the art would be able to prepare the 1:1 neutral complex of the Fe element and the glutamic acid from the teachings of Moore. The Examiner's assertion that Moore provides guidance to produce Applicants' 1:1 neutral complex appears to be based on an incorrect interpretation of Moore. The purpose of Moore is to prepare amino acid transition metal chelates homogeneously mixed with fatty acids to provide a source of transition metals for animal nutrition from lipoproteins and transition metal salts. (See column 2, lines 46-50). It is the resulting metal

chelates, preferably between 1.8 and 2.5 molecules of amino acid that is the purpose of Moore (see column 3, lines 17-25); a compound that is not a 1:1 neutral complex. It can hardly be said that where Moore's preferred embodiment is a metal chelate which is not neutral was obvious to the instant invention when the two are distinctly different compounds and of distinctly different utility.

The physical, chemical and biological properties of the neutral complexes described in the instant invention are significantly different than those of the aqueous mixture of amino acid transition metal chelates and fatty acids disclosed in Moore. Indeed, at column 1, lines 39-47, Moore draws the distinction between chelates and 1:1 complexes of α-amino acids: "The foregoing patents refer to complexes and not to chelates. Complexes are not necessarily chelates, but chelates are considered to be special ring structured metal complexes." This shows that the neutral complexes disclosed in the instant invention are not anticipated by Moore since they do not meet the requirements specified in the statement.

The claimed 1:1 neutral complexes of the instant invention as used for highly bioavailable trace element sources were discovered only after a multi-step, deliberate process to synthesize and select those with the desired properties of improved bioavailability, higher metal content, and excellent physical properties making them easier to manufacture, ship, store, and blend. The novel features of this use of the invention are not rendered obvious by Moore for the foregoing reasons. It simply does not suggest the compounds or the claimed use. Applicants respectfully request the Examiner to withdraw the ground for objection.

2. Claim Rejection – 35 U.S.C. § 103(a) - ICN

Claim 1 is rejected as unpatentable over ICN. Applicants respectfully traverse this rejection. It is the Examiner's assertion that although the instant invention differs from this prior

art in that the 1:1 neutral complex of an essential trace element and a dicarboxylic α-amino acid is recited, the ICN reference offers guidance that the synthetic amino diet composition can be adjusted depending on its use. The Examiner's assertion appears to have no correlation or relevance to the instant invention. The one-page ICN reference used by the Examiner is presumably from a catalog which offers purified Animal Research Diets. The Examiner appears to make a correlation between this reference and the instant invention because the reference contains the words "synthetic amino acid." As noted in the foregoing arguments, the instant invention required much more than looking at a reference containing the same words. The claimed 1:1 neutral complexes of this invention were discovered only after a multi-step, deliberate process to synthesize and select those with the desired properties of improved bioavailability, higher metal content, and excellent physical properties. It was not just a matter of changing a prior art ratio as suggested by the Examiner. Additionally, the Examiner's reference is silent as to any utility of the amino acid other than for a control diet. The reference does not provide guidance as to chemical, physical or nutritional properties. Nor does it suggest, one way or the other, the neutrality of the complex. The Examiner's argument that a person skilled in the art would arrive at the claimed complexes of the instant application and their novel features by looking at one page from the ICN catalog is without any legal merit. Claim 1 is therefore not rendered obvious by ICN and Applicants respectfully request that this ground of rejection be withdrawn.

V. Conclusion

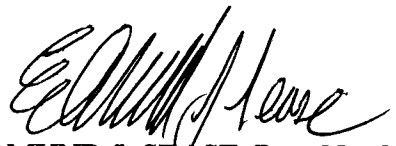
Applicant's Attorney has made a sincere effort to address specifically each of the Examiner's objections to claims 1 and 2 and to make amendments where appropriate in order to

place the claims in condition for allowance. For all of the above stated reasons it is believed the present application is now in condition for allowance which is respectfully requested.

Please consider this a two-month extension of time and charge Deposit Account No. 26-0084 the amount of $225.00 for this extension. No other fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



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Enclosures: Chinese translations
Cite 378 F.2d 959 (1967)

Zhang Youming[1], Bai Junfeng[1], Lu Manqing[1], Lu Airu[1]: Synthesis and Properties of Amino Acid Zinc Salts

Chemistry World, 1997, pp. 82-84

[1] Institute of Chemistry, Northwest Teacher's University, Lanzhou

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SYNTHESIS AND PROPERTIES OF AMINO ACID ZINC SALT

Abstract

This paper describes the synthesis of zinc aspartate and zinc glutamate by reacting L-aspartic acid and L-glutamic acid with zinc oxide. The conditions were mild. The yield was 95%. This method has potential developmental value.
Keywords: L-aspartic acid, amino acid zinc salt, zinc oxide

Zinc is one of the microelements essential to the human body. Zinc deficiency is a common problem [1]. Zinc sulfate is the main zinc-supplementing medicine, and has been used to treat stomachache, acne, anorexia, acrodermatitis enteropathica, gastric ulcers, infertility, eczema, hypoimmunity, ulcers of lower limbs, flu, and other diseases [2]. It, however, causes relatively serious side effects in the gastrointestinal tract. In some cases, it will cause bleeding in the stomach. Therefore, licorice zinc [3], zinc gluconate [4], and other zinc agents have been synthesized and have been widely used in clinical applications. Because of the peculiar physiological functions of amino acids, a product synthesized from an amino acid and zinc has synergistic effects beneficial to the human body. An amino acid zinc salt has the following major advantages: (1) with an amino acid used as an integration agent, it can help to treat hyperhydrochloria or peptic ulcers, (2) an amino acid contains N atoms with very strong negative electricity that can accept H+ protons and can treat ulcerative diseases [2]. Therefore, we synthesized solid compounds of zinc aspartate and zinc glutamate.

1 Experiment

1.1 Reagents: ZnO, L-aspartic acid, L-glutamic acid, all of which were analytically pure.

1.2 Instruments: Element analyzer: PE-2400.

IR analyzer: Alpha. Centauri FTIR

Electroconductivity meter: DDS-11A

1.3 Test method: C, H, N analysis was conducted according to conventional methods. The Zn content was determined by titration using EDTA.

1.4 Synthesis of compounds

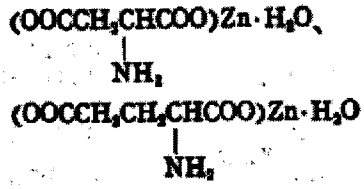
The amino acid and zinc oxide were weighed at a molar ratio of 1.25:1. The amino acid was dissolved in an appropriate amount of water. The ZnO powder was added in batches under stirring. When the pH of the solution reached 7, the insoluble content was filtered out. The filtrate was heated under reflux for 5-6 h and was then evaporated on a water bath until a film was formed. Then, methanol was added and stirring was performed. A solid was deposited. The

deposited solid was dried in a vacuum dryer and was then finely ground and weighed. The yield was 95%.

2 Results and discussion

2.1 Composition and properties of compounds

Table 1 shows the carbon, hydrogen, and nitrogen analytical results of the amino acid zinc compounds. As can be seen from the table, the compositions of the compounds were as follows:



Both of the aforementioned two amino acid zinc compounds were white powders, which were water soluble but were insoluble in methane.

Table 1 C, H, N analytical results and electroconductivity measurement results of amino acid zinc compounds

① 配合物	C%		H%		N%		Zn%		⑤ 电导测定	
	③ 理论值	④ 测值	③ 理论值	④ 测值	③ 理论值	④ 测值	③ 理论值	④ 测值	⑥ 溶液浓度	⑦ 摩尔电导
② 天冬氨酸锌	23.43	23.97	3.27	3.77	6.54	6.51	30.37	30.17	1.009×10^{-3}M	85.07
谷氨酸锌	26.32	26.80	3.65	3.49	6.14	6.56	28.51	28.46	1.004×10^{-3}M	83.67

Key:
1 Compound
2 Zinc aspartate
Zinc glutamate
3 Theoretical value
4 Measured value
5 Measurement of electroconductivity
6 Concentration of the solution
7 Molar electroconductivity

Table 2. IR vibration frequency of L-glutamic acid and the zinc compound thereof

			① L-谷氨酸	$(OOCCH_2CH_2CHCOO)Zn\cdot H_2O$
$-NH_3^+$的振动①	⑥	伸展振动	3106	3154
		反对称振动	1664	
		平面摇摆	1129	1096
$-COO^-$的振动②		反对称伸展	1581	1583
		对称伸展	1421	1413
		弯曲摇摆	871	
$-CH_2-CH_2-$的振动③		卷曲振动	1308	1307
$C<^{NH_3^+}_{COO^-}$的振动④		C—N^+伸展	1020	1043
H_2O的振动⑤		平面摇摆		814
		O—H振动		3380

Key: 1 Vibration of $-NH^{+3}$
1' L-glutamic acid
2 Vibration of –COO-
3 Vibration of $-CH_2-CH_2-$
4 Vibration of $C<^{NH_3^+}_{COO^-}$
5 Vibration of H_2O
6 Extended vibration
Antisymmetric vibration
Surface vibration
Antisymmetric extension
Symmetric extension
Flexural vibration
Curling vibration
$C-N^+$ extension
Surface vibration
O-H vibration

Water was used as the solvent to prepare a compound solution with a concentration of 1×10^{-3} M. The measured molar electroconductivity of zinc aspartate was 85.07 $S.cm^2 \cdot mol^{-1}$. The molar electroconductivity of zinc L-glutamate was 83.67 $S.cm^2 \cdot mol^{-1}$ (see Table 1). This meant that both of them were 1:1 compounds.

2.2 IR spectrum

Since both aspartic acid and glutamic acid are double-carboxyl acids and have a similar structure, the obtained two compounds have a similar IR spectrum. Compared with the ligand, some of the main absorption peaks have an obvious displacement, and the relative intensity is

also changed. This proves that a coordination effect occurs between Zn^{2+} and the amino acid. The absorption peaks of the symmetric extension of the carboxyl group in the compounds are at 1399 cm^{-1} and 1413 cm^{-1}, which are shifted to the low-frequency side by 8-22 cm^{-1} compared with 1421 cm^{-1} for the two amino acids. The extended vibration of NH^{+}_{3}shifts to the high frequency side and has an absorption peak of an M-O bond in the range of 500-600 cm^{-1}. These facts indicate that the amino acid in the compound is still present in the form of an inner salt. The oxygen atom in the carboxyl group forms bond with Zn^{2+}. The N atom does not participate in bonding. The displacement of the extended vibration of NH^{+}_{3} is caused by a hydrogen bond of H_2O. A relatively wide absorption peak is present near 3400 cm^{-1}, indicating the presence of water molecules in the compound [6].

Tables 2 and 3 show the IR spectral vibration frequencies of some groups of the ligands and the corresponding compounds.

Table 3. IR vibration frequency of aspartic acid and the zinc compound thereof

		① 天冬氨酸	$(OOCCH_2CHCOO)Zn\cdot H_2O$ $\vert$ NH_3
②$-NH^{+}_{3}$的振动	⑦ 伸展振动	80.6	3110
	反对称弯曲	1691	1717
	平面摇摆	1119	1119
③$-COO^{-}$的振动	反对称伸展	1606	1596
	对称伸展	1421	1399
	弯曲振动	657	689
④$-CH_2-$的振动	非平面摇摆振动	1367	1399
	卷曲振动	1308	1308
⑤ $C\langle^{NH^{+}_{3}}_{COO^{-}}$ 的振动	C—N^{+}伸展	1045	1016
⑥ H_2O的振动	C—C伸展	889	905
	平面摇摆		866
	O—H振动		3459

Key:
1 Aspartic acid
2 Vibration of –NH3+
3 Vibration of –COO-
4 Vibration of $-CH_2-CH_2-$
5 Vibration of $C\langle^{NH^{+}_{3}}_{COO^{-}}$
6 Vibration of H_2O
7 Extended vibration
Antisymmetric vibration
Surface vibration
Antisymmetric extension
Symmetric extension
Flexural vibration
Non-surface vibration

Curling vibration
C-N^+ extension
C-C extension
Surface vibration
O-H vibration

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6 [illegible], [illegible]. [illegible], 1990; 20(增刊):116

Li Shiang-de[1], Li Yi, Mo Li-er,[1] Cheng He-feng,[1] Guang Xiong-tai,[2] Dongye Guangzhi[2]: Study on the Best Conditions for Preparation of Zinc Glutamate
Guangdong Trace Element Science, Vol. 8, No. 12, 54-57 (2001)

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STUDY ON THE BEST CONDITIONS FOR PREPARATION OF ZINC GLUTAMATE

Abstract: The synthesis of zinc glutamate by sodium glutamate and zinc oxide is reported. The raw materials are easily available. The conditions are mild. The operations in simple. The yield is of 86%. So the line of synthesis has potential application value.

Key words: sodium glutamate; zinc glutamate; synthesis

Figure classification No. TQ462.12 Reference Index Code: A

Zinc is one of the essential trace elements in the human body and a key element for maintaining normal body metabolism. Zinc deficiency is a common phenomenon. According to several surveys on child nutritional conditions conducted in China, about 26%-27% of the children showed a zinc deficiency; zinc deficient symptoms were also found in adults and seniors in some areas. Zinc deficiency in children adversely affects intelligence development and growth [1], and zinc deficiency in adults and seniors affects normal metabolism and reduces the immune system, resulting in the onset of disease.

The earliest zinc supplement utilized in food and medicine was zinc sulfate, but it irritates the gastric membrane and induces nausea and vomiting so that it is no longer used as a drug or nutritional supplement. Later on, zinc acetate, zinc citrate and zinc orotate – arginate were gradually developed in China and abroad. However, the demand by society could not be easily satisfied, and Japan successfully developed and commercialized zinc gluconate in 1979, which was clinically proven to have good therapeutic efficacy. Zinc glycyrrhizinate was developed and commercialized in this country in 1984, but China has a large population with individual differences in various areas and different requirements for zinc supplements, and the demand by society could not be met easily. A preliminary survey showed that there are not many zinc supplement products or varieties on the market, and that new products are in urgent demand. A survey of domestic literature for the last dozen years revealed that zinc glutamate exhibits very low toxicity (almost non-toxic) in acute, subacute and chronic toxicity studies and high bioavailability (about 66%) while all pharmacokinetic parameters fall in an ideal model [2]. Its efficacy as a zinc supplement was compared with that of zinc gluconate and the result showed that zinc glutamate is superior to zinc gluconate and the bioavailability is also higher than that of zinc gluconate while inducing no gastric irritation. Accordingly, the business need to study zinc glutamate as a medicinal nutrient and food is equal to the need to develop scientific research of nutritional trace elements. The authors synthesized solid complexes of zinc glutamate and investigated in detail the factors influencing the synthesis reaction and obtained the optimum processing conditions for synthesizing zinc glutamate.

1 Experimental

1.1 Key starting materials

Sodium glutamate (food grade sodium glutamate, content > 99%); zinc oxide (analytical grade); hydrochloric acid (analytical grade); methanol (analytical grade).

1.2 Synthesis of the product

Sodium glutamate and zinc oxide were weighed respectively at a molar ratio of 1.2:1, the sodium glutamate was first dissolved in a suitable amount of water, the mixture was placed in a water bath at 60°C, 6 mol/L hydrochloric acid were added while agitating until the pH was 3-4, and the result was then chilled. Subsequently, a suitable amount of water was added to the obtained solid glutamic acid, zinc oxide was added in increments while agitating, and this was then reacted for 5 h under agitation in a water bath at 90°C, followed by cooling and filtering The filtrate was subjected to evaporation in a water bath until the volume was reduced to 1/3, and a suitable amount of methanol was added, resulting in precipitation of solids, which were dried in a dryer under vacuum to obtain zinc glutamate as a white powder, which was weighed. Yield 86%.

2 Results and discussion

2.1 Composition analysis of zinc glutamate

2.1.1 Elemental analysis

Elemental analysis for carbon, hydrogen and nitrogen of the zinc glutamate complex was performed by conventional methods; the zinc content was determined by EDTA titration, and the analytical values were almost identical to the calculated values. Table 1 shows the analytical results.

Table 1. Values of elemental analysis of zinc glutamate complex (%)

	C	H	N	Zn
① 理论值	26.29	3.09	6.13	28.63
② 实测值	26.65	3.43	6.52	28.53

Key: 1 Calculated value
2 Analytical value

2.1.2 Test of molar conductivity

A 1 x 10^{-3} mol/L^{-1} solution (using H_2O as solvent) of the complex was prepared from the product, and the molar conductivity of the zinc glutamate was found to be 84.25 S·cm^2/mol^{-1}, suggesting that it was a 1:1 complex. Combining the analytical result in Table 1, the composition was validated as follows:

$$(OOCCHCH_2CH_2COO)Zn \cdot H_2O$$
$$\quad\quad|$$
$$\quad NH_2$$

2.1.3 Infrared spectrum [3]

Figure 1 and Figure 2 show the infrared spectra of zinc glutamate.

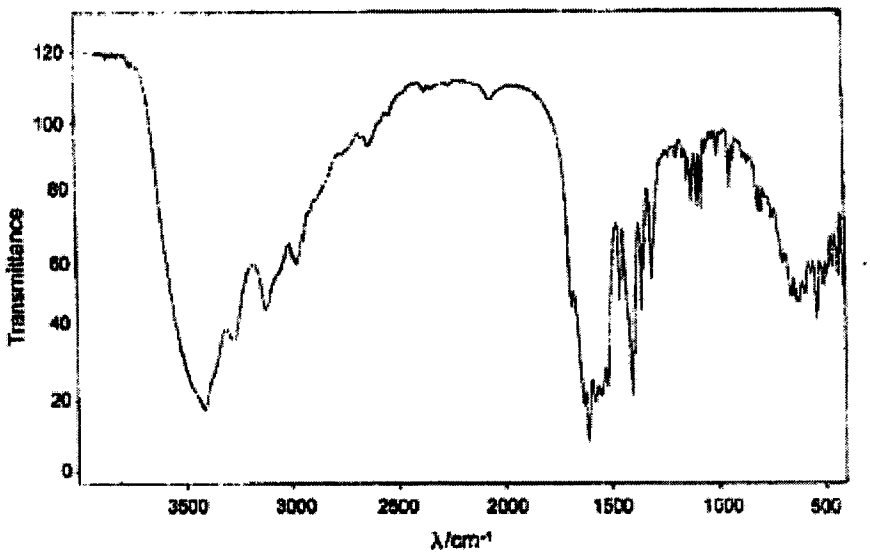


Figure 1. Infrared spectrum of zinc glutamate product

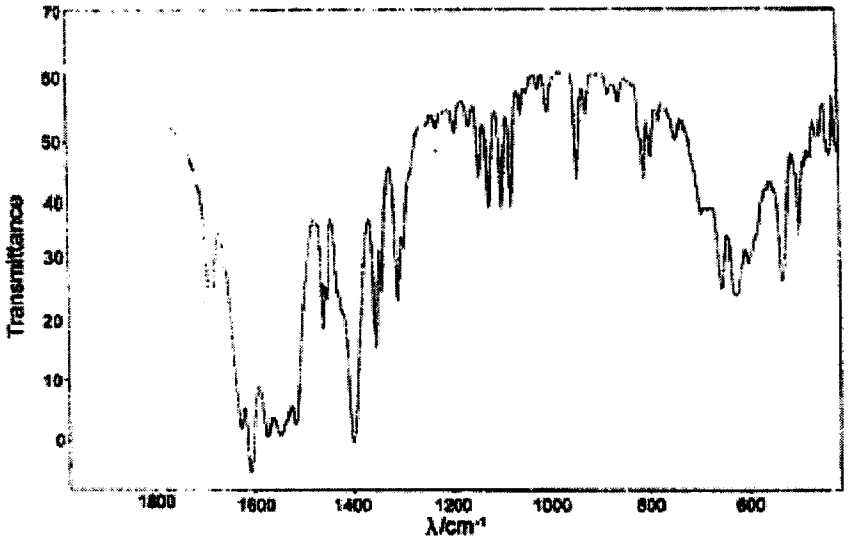


Figure 2. Infrared spectrum of zinc glutamate product (400-1800 cm^{-1})

Figure 1 and Figure 2 show that the key absorption peaks of the structure may be assigned as follows: the strong and broad absorption peak at 3300-3550 cm^{-1} belongs to the stretching vibration of the OH of the crystalline water, the peak at 3300 cm^{-1} is the NH stretching vibration, 2870 cm^{-1} is the CH_2 stretching vibration, 1300 cm^{-1} is the CH_2 bending vibration, 1680 cm^{-1} is the stretching vibration for the carbon in COO, in which the electron cloud density on the carbon-oxygen bond is reduced so that the absorption peak shifts to a low frequency, and 1610 cm^{-1} and 1400 cm^{-1} are the asymmetric stretching and symmetric stretching vibrations for COO, 1100 cm^{-1} is the C-N stretching vibration and 810 cm^{-1} is the N-H out-of-plane bending vibration while 670, 580 and 550 cm^{-1} are stretching vibrations for O-Zn.

2.2 Influence of synthesis condition of zinc glutamate on yield

The influences of various factors including the molar ratio of sodium glutamate to zinc oxide, the reaction time and the reaction temperature on the yield of the synthesis of zinc glutamate during the process of preparing the product were investigated by comparative studies.

2.2.1 Influence of molar ratio of reactants on yield

Table 2 shows the influence of the molar ratio of the reactants on the yield at the reaction conditions of reaction time 5 h, reaction temperature 90°C and crystallizing time 7 h.

Table 2. Influence of the molar ratio of sodium glutamate to zinc oxide on yield

① 谷氨酸钠：氧化锌（摩尔比）	产率/% ②
1.0:1	83.7
1.2:1	86.2
1.4:1	86.4
1.6:1	86.3

Key: 1 Sodium glutamate:zinc oxide (molar ratio)
2 Yield

Table 2 reveals that the optimal molar ratio of sodium glutamate to zinc oxide is 1.2:1 based on the yield and the material costs.

2.2.2 Influence of reaction time on yield

Table 3 shows the influence of the reaction time on the yield at the reaction conditions of molar ratio of sodium glutamate to zinc oxide 1.2:1, reaction temperature 90°C and crystallizing time 7 h.

Table 3. Influence of reaction time on yield

① 反应时间/h	产率/% ②
1.0	69.5
3.0	82.3
5.0	86.1
7.0	86.5

Key: 1 Reaction time
2 Yield

The results revealed that the yield of zinc glutamate increased with increasing reaction time, and the yield reached a maximum at a reaction time of 5 h, but when the reaction time was further increased, the yield decreased; thus 5 h is the optimum reaction time.

2.2.3 Influence of reaction temperature on yield

Table 4 shows the influence of the reaction temperature on the yield at the reaction conditions of molar ratio of sodium glutamate to zinc oxide 1.2:1, reaction time 5 h and crystallizing time 7 h.

Table 4. Influence of reaction temperature on yield

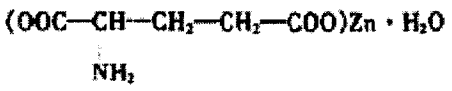
① 反应温度/℃	产率/% ②
70	76.5
80	83.6
90	86.2
100	86.3

Key: 1 Reaction temperature
2 Yield

The result revealed that the yield of zinc glutamate increased with increasing reaction temperature, and the yield reached a maximum at a reaction temperature of 90°C, but when the reaction time was further increased, the yield showed little changes; thus 90°C is the optimum reaction temperature.

3 Conclusion

(1) Combining the elemental analysis, test of molar conductivity and infrared analysis, the composition was validated as follows:



(2) The optimum synthetic conditions for zinc glutamate are a molar ratio of sodium glutamate to zinc oxide of 1.2:1, reaction time of 5 h, reaction temperature of 90°C and crystallizing time of 7 h.

References

[1] 王夔主编. 生命科学中的微量元素（下卷）[M]. 北京：中国计量出版社，1992. 98.
[2] 郎仁英等. 中国医药工业杂志，1992，23 (3)：114~115.
[3] 陈德恒. 有机结构分析 [M]. 北京：科学出版社，1985. 128.

35 U.S.C. § 103, the latter including prior invention under 35 U.S.C. § 102(g). Although "all" subject matter which is clearly common to the applications of the winning and losing interference parties may be used for purposes of an interference estoppel rejection against the losing party's claims, the extent to which this commonly disclosed subject matter may be used as available evidence of the "prior art" under section 103 depends on whether the common subject matter relied on meets one or more of the paragraphs of 35 U.S.C. § 102. This, of course, will in turn depend on the facts and circumstances of a particular case. General rules, e. g. that "all" commonly disclosed subject matter is "prior art" against the losing party's claims, In re Boileau, supra, are to be neither trusted nor blindly applied in particular cases in which the facts may well differ materially from the controlling facts in precedents wherein such generalities are expressed.

For the reasons stated above, the decision of the board in PA 7574 is reversed as to the subgeneric claim 44 and affirmed as to species claim 47, and the appeal in PA 7677 is dismissed as moot.

MODIFIED

WORLEY, C. J., concurs in the result.

MARTIN, J., participated in the hearing of this case but died before a decision was reached.

SMITH, Judge (concurring).

The record shows that the Board of Appeals here consisted of an examiner-in-chief and two acting examiners-in-chief. Appellants do not challenge the legality of that board. For the reasons expressed in my dissenting opinion in In re Wiechert, 370 F.2d 927, 54 CCPA 957, the decision of such a board in my view is a legal nullity. However, I must accept the majority's view on this issue in the *Wiechert* case, i. e., the legality of the board is not an issue here. I therefore participate in the merits of this appeal and in so doing, agree with the conclusion of the majority.

54 CCPA

Application of Max J. KALM.

Patent Appeal No. 7698.

United States Court of Customs and Patent Appeals.

June 15, 1967.

Proceeding on application for patent with relation to invention concerning particular morpholine derivatives of a specified formula. The Patent Office Board of Appeals, Serial No. 803,847, affirmed examiner's rejection of certain claims as anticipated by certain prior art, and applicant appealed. The Court of Customs and Patent Appeals, Worley, Chief Judge, held that the genus disclosed by patent which revealed process for preparation of compounds exhibiting marked psycho-stimulating and appetite reducing effect were sufficiently narrow so as not to encompass compounds within scope of applicant's claims disclosing compounds to be useful as selective central nervous system depressants, and the application was not anticipated by the patent.

Reversed.

1. Patents ⇐66(1)

Rejection of patent application under statute as anticipated by prior art implies that the invention sought to be patented has been described in a patent granted on another application filed in United States before invention thereof by the later applicant and therefore is not new, that there are no differences between what is claimed and what is disclosed in the prior art. 35 U.S.C.A. §§ 102(e), 103.

2. Patents ⇐66(1)

A description in a reference which is insufficient to render composition of matter obvious to one of ordinary skill in the art is insufficient to "describe" the composition within statute providing that a person shall be entitled to a patent unless the invention was described in a patent granted on another's application

filed in United States before invention by the later applicant. 35 U.S.C.A. § 102 (e).

See publication Words and Phrases for other judicial constructions and definitions.

3. Patents ⇐58

A party seeking to claim the very same compound or composition as that specifically named and identified in a patent already issued must prove that the patent description was erroneous and that what the patent at first blush appears to expressly describe never actually existed. 35 U.S.C.A. §§ 103 and (e), 282.

4. Patents ⇐66(1.24)

The genus disclosed by patent which revealed process for preparation of compounds exhibiting marked psycho-stimulating and appetite reducing effect were sufficiently narrow so as not to encompass compounds within scope of applicant's claims disclosing compounds to be useful as selective central nervous system depressants, and the application was not anticipated by the patent. 35 U.S.C.A. § 102(e).

5. Patents ⇐66(1.12)

Disclosure of every property or attribute of a composition of matter is not necessary for a reference to be valid anticipation. 35 U.S.C.A. § 102(e).

Helmuth A. Wegner, Chicago, Ill., for appellant.

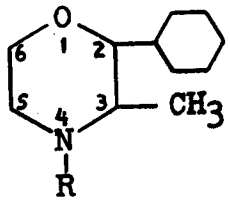
Joseph Schimmel, Washington, D. C. (Jack E. Armore, Washington, D. C., of counsel), for the Commissioner of Patents.

Before WORLEY, Chief Judge, RICH, SMITH and ALMOND, Judges, and WILLIAM H. KIRKPATRICK.*

WORLEY, Chief Judge.

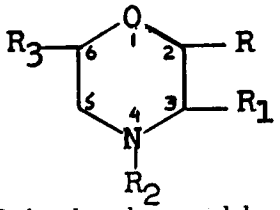
This appeal is from the decision of the Board of Appeals affirming the examiner's rejection of claims 1–3 [1] as anticipated by certain prior art under 35 U.S.C. § 102(e).

The invention relates to particular morpholine derivatives of the formula



wherein R for purposes here is lower alkyl, being so defined in claim 1 and 2. Claim 3 is directed to the specific compound 2-cyclohexyl-3, 4-dimethylmorpholine. According to the specification, the compounds are useful as "selective central nervous system [CNS] *depressants* —being potent barbiturate potentiators." (Emphasis supplied.)

A brief chronology of the proceedings below will facilitate an understanding of the issue involved. The examiner originally rejected claims 1–3 as "obvious to one having ordinary skill in the art. 35 U.S.C. 103" in view of the Siemer patent.[2] Siemer discloses a process for the preparation of compounds of the generic formula



where R is phenyl or cyclohexyl, R_1 is lower alkyl, and R_2 and R_3 may be hydrogen or lower alkyl,[3] as well as a "one

* Senior District Judge, Eastern District of Pennsylvania, sitting by designation.

1. Appearing in Serial No. 803,847, filed April 3, 1959, entitled "3,4-Dialkyl-2-Cycloalkylmorpholines and Congeners."

2. U.S. patent No. 3,125,572, issued March 17, 1964, on an application filed July 23, 1958.

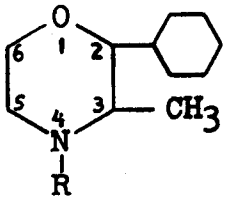
3. The only specific compounds disclosed by Siemer are 2-phenyl-3-methyl-morpholine, 2-phenyl-3, 4-dimethyl-morpholine, 2-phenyl-3-6-dimethylmorpholine, 2-phenyl-3-propyl-morpholine, and 2-cyclohexyl-3-methyl-morpholine, none of which falls within the ambit of appellant's claims.

ERIES

Y, Chief Judge.

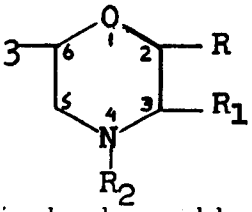
eal is from the decision of the Appeals affirming the examination of claims 1–3 [1] as anticipated by certain prior art under 35 02(e).

vention relates to particular derivatives of the formula



for purposes here is lower g so defined in claim 1 and 2. directed to the specific com- clohexyl-3, 4-dimethylmorpho- rding to the specification, the are useful as "selective cen- us system [CNS] *depressants* tent barbiturate potentiators." supplied.)

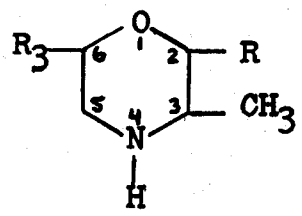
chronology of the proceedings facilitate an understanding of involved. The examiner orig- cted claims 1–3 as "obvious to ordinary skill in the art. 35 " in view of the Siemer pat- ner discloses a process for the n of compounds of the generic



is phenyl or cyclohexyl, R_1 is l, and R_2 and R_3 may be hy- lower alkyl,[3] as well as a "one

[3] specific compounds disclosed by re 2-phenyl-3-methyl-morpholine, 3, 4-dimethyl-morpholine, 2- 6-dimethylmorpholine, 2-phenyl- morpholine, and 2-cyclohexyl-3- orpholine, none of which falls e ambit of appellant's claims.

step" process for preparing compounds of the formula



According to Siemer, the compounds he discloses

> * * * exhibit a marked psychostimulating and appetite reducing effect. The morpholines that are substituted in 2, 3 position, as for example 2-phenyl-3-methylmorpholine [4] and 2-cyclohexyl-3-methylmorpholine have a *most marked anti-depressive action.* * * * (Emphasis supplied.)

The examiner predicated his § 103 rejection particularly on the latter compound, 2-cyclohexyl-3-methyl-morpholine, which differs structurally from the compounds of claims 1–3 in the absence of a methyl or other lower alkyl group in the 4-position of the morpholine nucleus.

In response to the examiner's rejection, appellant submitted an affidavit of a Dr. Drill (Drill I) under Rule 132, reporting the results of assays conducted to determine the effect of four compounds on the central nervous system. The compounds tested were the compound of claim 3 and 2 -cyclohexyl- 3 -methyl- 4 -octylmorpholine hydrochloride (the latter falling within the scope of claims 1 and 2), as well as the two specific compounds to which Siemer attributes marked antidepressive action. Drill concluded from the reported data that the reference compounds "2-cyclohexyl-3-methyl-morpholine and the corresponding 2-phenyl compound, Preludin, produced a *significantly stimulating* (95% Conf.) effect on the central nervous system," whereas the two compounds falling within the present claims "*depressed* the central nervous system."

Appellant also submitted his own affidavit, laboratory notebook exhibits, and biological testing reports under Rule 131, reporting that he had synthesized the 4-methyl compound of claim 3 and the 4-octyl compound heretofore mentioned, submitted them to pharmacological evaluation, and established "their depressant effect upon the central nervous system" in "standardized assays," all prior to July 23, 1958, the filing date of Siemer.

Subsequently, the examiner accepted the Drill I affidavit under Rule 132, finding it "to be sufficient to show a difference in kind in an evaluation of pharmacological properties as between the claimed compounds and the N-unsubstituted amines specifically disclosed by the reference," and conceded that "the instant compounds would be rendered unobvious by the Rule 132 affidavit and hence patentable. In re Papesch, [50 CCPA 1084, 315 F.2d 381,] 137 U.S.P.Q. 43." However, the examiner then proceeded to reject claims 1–3 as "fully met by Siemer," stating:

> * * * The reference is considered to so completely describe the claimed morpholines as to negate patentability with[in] the meaning of 35 U.S.C. 102 (e). The reference discloses a narrow generic teaching of the claimed amines as well as a method for preparing the compounds. Also an N-homologue [the examiner was here referring to the 2-cyclohexyl-3-methylmorpholine compound on which he originally predicated his § 103 rejection] * * * is described specifically in example 7. These disclosures by the patentee, it is submitted, are sufficient to negate patentability of the claimed amines within the test laid down in In re Petering, * * * [49 CCPA 993, 301 F.2d 676, 133 U.S.P.Q. 275].

He accepted appellant's Rule 131 affidavit "to the extent that preparation of the compounds is described therein" and as evidence of "clear conception" of those

[4.] It appears from the record that 2-phenyl-3-methyl-morpholine is marketed under the name "Preludin" as a CNS stimulant.

compounds, but found it, for various reasons, to be "unacceptable to prove a *successful* reduction to practice," i. e., appellant had not satisfactorily established the "usefulness" of the compounds prior to the filing date of the Siemer reference.

The board agreed with the examiner's rejection of the claims under 35 U.S.C. § 102(e), finding that the

> * * * reasoning of the court in In re Petering * * * is clearly applicable here to establish the anticipatory effect of the Siemer et al. disclosure.

It also agreed with the examiner that it was necessary for appellant to show that he knew of a use for his compounds prior to the filing date of Siemer in order to overcome Siemer as a reference since, according to the board, the patentee discloses "therapeutic utility" for the compounds; that appellant's Rule 131 affidavit was inadequate to establish that he had found a use prior to the filing date of Siemer; and that, as a consequence, appellant had not shown he was prima facie the first inventor of the claimed subject matter.

[1] A rejection under 35 U.S.C. § 102(e) for anticipation, such as made by the Patent Office in the present case, necessarily implies that the invention sought to be patented has been "described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent," and therefore is not "new"—that there are no differences between what is claimed and what is disclosed in the prior art. Even where there are differences, "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103.

In making his original rejection under § 103, the examiner was faced with readily apparent differences between the subject matter "sought to be patented" and the prior art, viz. the claimed compounds are central nervous system *depressants* while the disclosed compounds of Siemer are central nervous system *stimulants*. The examiner, considering those differences, found appellant's narrow group of compounds to be unobvious, § 103, to one of ordinary skill in the art, notwithstanding the Siemer reference.

[2] Bearing that determination in mind, it is somewhat difficult for us to comprehend how appellant's compounds may be *unobvious* in view of a reference, yet at the same time be said to be *described* by the same reference as the Patent Office has held here. Necessarily, a description in a reference which is insufficient as a matter of law to render a composition of matter obvious to one of ordinary skill in the art would a fortiori be insufficient to "describe" the composition as that term is used in 35 U.S.C. § 102(e), a complete description being but the ultimate or epitome of obviousness.

[3] There appears to be no question that the Siemer patent does not specifically name, describe or claim any particular, individual compound anticipating appellant's claims, nor is there any suggestion by Siemer that *any* of his disclosed compounds is capable of *depressing* the central nervous system. Thus, this is not a case where a reference patent imputes particular characteristics to a readily prepared, *specifically named* and *identified* compound or composition, and a party seeking to claim the *very same* compound or composition must prove that the patent description was erroneous and that what the patent at first blush appears to expressly describe never actually existed. Cf. 35 U.S.C. § 282; In re Molnar, 366 F.2d 782, 54 CCPA 705; In re Jacobs, 318 F.2d 743, 50 CCPA 1316.

[4] It is the position of the Patent Office that the presently claimed compounds fall within the scope of the

"genus" disclosed by Siemer. A cursory inspection of the Siemer reference might lead one to that unwarranted conclusion. The solicitor asks that we look at the specific exemplary compounds of Siemer [3] in order to determine the substituents he preferred and to establish the narrow scope of his generic disclosure. We have done so. If any preference of Siemer can be ascertaned, it is for compounds with a phenyl radical in the 2-position, a methyl radical in the 3-position and hydrogen in the 4-position of the morpholine nucleus, yielding the commercial stimulant "Preludin." Only when phenyl appears in the 2-position does Siemer disclose that methyl may be present in positions 4 or 6; only when methyl is in position 3 and hydrogen is in position 4 does Siemer suggest that cyclohexyl may appear in position 2. No real intimation is made as to what would happen if cyclohexyl, methyl and methyl were *simultaneously* placed in positions 2, 3 and 4, respectively. Siemer's disclosure *is* narrow. The genus constructed with the aid of Siemer's examples is much narrower than that which is depicted in a shorthand manner by Siemer's "generic" chemical formula appearing earlier in this opinion. Indeed, we think that the "genus" disclosed by Siemer is sufficiently narrow that it does not encompass compounds within the scope of appellant's claims. See E. I. duPont de Nemours & Co. v. Ladd, 117 U.S.App.D.C. 246, 328 F.2d 547.

[5] When one speaks of a "genus" in the chemical arts, one ordinarily speaks of a group of compounds closely related both in structure and in properties. Appellant has found a group of chemical compounds which possess properties diametrically opposite to the properties disclosed by Siemer for his compounds. It is quite evident that Siemer never made the present compounds; or if he did, he never tested them to determine what effect they would have on the central nervous system, since, if he had, he could not logically have failed to report the seemingly anomalous result appellant has discovered. While it is not necessary that a reference disclose every property or attribute of a composition of matter to be a valid anticipation, appellant has found properties for his claimed compounds which are totally incompatible and inconsistent with, not merely complementary or in addition to, those attributed by Siemer to his compounds. It is our view that Siemer never intended to, nor does he, disclose compounds within the scope of appellant's claims.

The examiner, board and solicitor rely heavily on this court's decision in In re Petering. We had occasion to comment upon some limitations of that decision in In re Ruschig, 343 F.2d 965, 52 CCPA 1238, where we stated:

> We did not intend our *Petering* opinion or decision to become a precedent for the mechanistic dissection and recombination of the components of the specific illustrative compounds in every chemical reference containing them, to create hindsight anticipations with the guidance of an applicant's disclosures, on the theory that such reconstructed disclosures *describe* specific compounds within the meaning of section 102. * * *

Contrary to the solicitor's position here, the compounds which are allegedly encompassed by the general disclosure of Siemer do not constitute a "recognizable class *with common properties*," *Ruschig*. As in *Ruschig*, the number of compounds which could be said to fall within the scope of Siemer's disclosure, considering all possible permutations and combinations, is far greater than the 20 compounds found to be disclosed by the reference in *Petering*. We do not consider the situation in *Petering* comparable to that here.

The view we take renders it unnecessary to consider appellant's evidence submitted under Rule 131, and the parties' arguments directed thereto.

The decision is reversed.

Reversed.

SMITH, J., concurs in the result.